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Student Number:**

Advanced Medical Science Research Report

**The Risk of Subsequent Events,
Etiology and Yield of Diagnostic
Testing in Patients Admitted for an
Apparent Life-Threatening Event.**

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STATEMENT FROM SUPERVISOR

This research project has been approved and is ready for submission

Marc N. Baskin, M.D
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Date

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First I would like to thank my supervisor, Marc Baskin, for allowing me to take on such a great project. His help in all aspects of the project was integral to its final form. Also his assistance in broadening my outlook on the role of clinical research in medicine is greatly appreciated.

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And finally, to my girlfriend, friends and family for their unparalleled support, especially to those who traveled half way around the world to see me.

ABSTRACT

THE RISK OF SUBSEQUENT EVENTS, ETIOLOGY AND YIELD OF DIAGNOSTIC TESTING IN PATIENTS ADMITTED FOR AN APPARENT LIFE-THREATENING EVENT (ALTE).

BACKGROUND: For infants with an ALTE, the length of stay (LOS) necessary to prevent morbidity is unknown and little data exists on the yield of diagnostic testing.

OBJECTIVE: To describe the risk of subsequent events, etiology and yield of diagnostic testing in infants admitted for an ALTE.

DESIGN/METHODS: Retrospective chart review of consecutive infants < 1 year of age admitted to a tertiary children's hospital due to an ALTE between October 1995 and September 2003. Cases were identified by electronically searching the Emergency Department (ED) record for the words 'apnea', 'limp', 'cyanosis', 'choke' and 'pale'. Additionally the entire ED record was searched for the acronym 'ALTE'. Serious events were defined as the occurrence of cyanosis, apnea, seizure, oxygen saturation \leq 90%, limpness, unresponsiveness or death. Cases were crosschecked with the Massachusetts Center for Sudden Infant Death Syndrome (SIDS) database for post discharge mortality.

RESULTS: 1039 patients were identified and 994 (95%) charts reviewed. 166 were excluded because their history was not consistent with an ALTE. Of the 828 cases, 267 were managed as outpatients and 561 were admitted.

135 / 561 (24%) patients had a serious event during their hospitalization. Most serious events were some combination of oxygen desaturation and apnea or cyanosis. 6 patients had seizures and there were no deaths. The events occurred a median of 7.7 hours after admission and only 14 patients (2.5%) had a first serious event > 24 hours after admission. Patients who were not ill appearing, had no events in the emergency department and were not admitted to an ICU were at low risk for serious events, relative risk 0.28 (95% Confidence Interval (CI) 0.22, 0.37). Patients with only one event prior to presentation and a gestational age of ≥ 35 weeks were also at reduced risk. 47% of patients were discharged without a clear etiology. The most common causes were gastroesophageal reflux (28%) and bronchiolitis (8.0%). 5.2% of patients had a life threatening condition diagnosed. There were 12 seizures, 8 cases of pertussis and 2 of abuse.

Of the 9 ED tests performed in more than 25% of our sample, only chest radiographs had a yield of >2.5%. Some more infrequently performed tests had a higher yield, pertussis PCR (38%), RSV antigen detection (31%), airway films (25%) and arterial and venous blood gases (both 13%).

There was no post discharge mortality from SIDS.

CONCLUSIONS: The risk of serious events was sufficient to warrant observation in all patients, and a LOS of 24 hours was appropriate for safe evaluation of those at low risk for repeat events. One in 20 patients had a life

threatening condition diagnosed and the yield of emergency department testing was low.

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BACKGROUND

INTRODUCTION

In 1986 the National Institutes of Health (NIH) Consensus Development Conference on Infantile Apnea and Home Monitoring (1) defined an Apparent Life-Threatening Event (ALTE) as:

An episode that is frightening to the observer and is characterized by some combination of apnea (central or occasionally obstructive), color change (usually cyanotic but occasionally erythematous or plethoric), marked change in muscle tone (usually marked limpness), choking, or gagging.

In some cases the observer fears that the infant has died.

This definition was introduced to standardize research into ALTEs, and to alleviate the potential confusion created by the use of ambiguous terminology such as “aborted crib death” or “near miss SIDS”.

As outlined by a number of authors (2-6), studying the epidemiology of ALTEs is problematic because there is a marked heterogeneity of clinical presentation and the definition has a large subjective component. No published data exist on the reliability of caregiver reporting of ALTEs in unmonitored infants. In monitored infants, the data suggests caregiver reporting is neither sensitive nor specific for true events (7, 8).

While apparent life-threatening events have been described in older children (9), the vast majority occur in children less than one year of age. The median age is 40 – 84 days (4, 5, 10-17).

Infants presenting after an apparent life-threatening event represent a management dilemma for both emergency physicians and pediatricians. The frequently normal physical examination, diverse range of etiologies and undetermined risk of subsequent events make the choice of diagnostic testing and duration of admission difficult.

INCIDENCE

Various studies have estimated the incidence of ALTE to be between 0.5% and 6% (18-21). The wide range of these results reflects the use of differing criteria for the event. For example the 4% - 6% estimates were from studies in which parents were asked if their child had ever turned blue (19). These studies included children for whom no medical attention was sought and thus overestimate the true incidence of events that are 'frightening to the observer'. Conversely, the lower values may underestimate the true incidence because their criteria is too strict, for example requiring the event to occur in the first 4 days of life (20), or during sleep and requiring vigorous stimulation or cardiopulmonary resuscitation (18).

ETIOLOGY

The 1986 NIH consensus statement describes an ALTE as a “chief complaint that describes a general clinical syndrome” (1). Thus the syndrome may be due to a specific etiology or remain idiopathic. Due to the inclusive nature of the definition, the differential diagnosis for an ALTE is extensive. Numerous studies have been conducted examining the etiological diagnoses after an ALTE has occurred. The most common causes are listed in Table 1. The estimated proportion is the average of the percentages obtained in previous studies, weighted by sample size.

Additionally, many less frequent etiologies have been described, such as colic medication (22), myocarditis (23), intrapulmonary shunting (24), poisoning (25, 26) or inborn errors of metabolism (27, 28). Meningitis and bacteremia are also rare causes, accounting for 0-1% of cases (11, 14, 15).

Table 1: Previous Research on ALTE Etiology

Etiology	Estimated Proportion	Range of Estimates	References
Idiopathic	32%	15 – 54%	(11, 12, 14-16, 29-33)
Gastroesophageal Reflux	38%	16 – 62%	(11, 14-16, 30-33)
Lower Respiratory Infection (Inc Bronchiolitis)	12%	4 – 20%	(11, 14-16, 30)
Seizure	8%	1 – 25%	(11, 12, 14-16, 30, 31)
Pertussis	4%	1 – 9%	(11, 15, 16, 33)
URI	3%	2 – 4%	(11, 14, 15)
Abuse	3%	0 – 11%	(11, 12, 14-16, 31, 33)
Factitious Illness (Munchausen’s by Proxy)	1%	0 – 4%	(11, 12, 14-16, 31, 33)

EMERGENCY DEPARTMENT DIAGNOSTIC TESTING

A number of review papers provide suggestions for the appropriate diagnostic testing in patients who present after an ALTE (2, 6, 17, 34, 35). Such recommendations, however, do not have a firm empirical foundation. In fact, previous studies have found that, although a large number of tests are often performed (13, 15, 16, 36), they are of little utility (Table 2).

Table 2: Previous Data on ED Testing Utility

Study	Number of Patients	Utility	Definition of Utility used in study
Lewis 1986 (13)	125	3.2%	Useful in diagnosis or treatment
Gray 1999 (15)	196*	0%	Clearly influence proposed management
De Piero 2004 (36)	122	2.5%	Led to a diagnosis

* Represent total number of patients in study, only a small proportion received testing.

Both studies that found utility did so in patients with signs or symptoms suggesting the diagnosis.

RISK OF SUBSEQUENT EVENTS

Infants who have an ALTE are perceived to be at risk of having another event, both during their hospitalization and after discharge. The risk of further events is often one of the reasons these infants are admitted (6, 17, 35). Thus quantifying the risk of subsequent events and their timing is integral in determining the length of hospital stay necessary to evaluate patients after an ALTE. The identification of predictive variables for subsequent events would allow physicians to assess the individual patient's risk more accurately.

Two studies have examined the risk of subsequent events during hospitalization. One study found that 7.8% of patients admitted for an ALTE will require significant medical intervention during their hospitalization (36). Samuels and colleagues (12) found that 35% of patients have abnormalities of oxygenation during hospitalization. Their sample, however, was restricted to infants who received mouth-to-mouth resuscitation for their initial event and had a higher proportion of cases due to intentional injury (11%) and factitious illness (4%) than most other studies.

As important as it is to know the absolute risk of having a further event, it is perhaps more important to know when these events are likely to occur. This information could help determine the hospital length of stay necessary to safely evaluate these patients. No previous studies have evaluated when subsequent events are likely to occur.

PREDICTORS OF SUBSEQUENT EVENTS

Only one study has looked for predictive variables of serious events during hospitalization. De Piero and colleagues (36) found that prematurity, a positive medical history (defined as carrying a specific diagnosis such as gastroesophageal reflux or tracheomalacia) and an age of less than 60 days all increased the likelihood of subsequent events. Other studies have been performed using events at home as the outcome of interest. Steinschneider and colleagues (4) found that no variables relating to the initial ALTE

presentation predicted subsequent events with statistical significance. Likewise Dunne et. al. (5) found no predictors, despite the fact that 41% of their sample had repeat episodes at home. The only previously described predictor of recurrent home events was the occurrence of an event during admission (37). This affirms the need for more research into events occurring during hospitalization.

RELATIONSHIP TO SIDS

Although the biological link between apparent life-threatening events and sudden infant death syndrome is unknown, many papers have been published on the potential epidemiological association. Most studies report a prior incidence of an ALTE in SIDS victims of 5 to 10% (8, 18, 38, 39), however the lack of controls in these studies limits the strength of their conclusion. Mitchell and Thompson (21) found that infants who had ever stopped breathing for greater than 20 seconds had a significantly increased risk of SIDS compared to infants who had no such events. All of these studies were retrospective and thus these results may be the effect of recall bias.

OBECTIVES

The primary objectives of this study were to:

1. To describe the risk and timing of serious events during hospitalization in patients admitted for an ALTE.
2. To determine the etiology of the ALTE, and the proportion of diagnoses that are life threatening.

The secondary objectives were to:

1. To determine the utilization and yield of diagnostic testing.
2. To determine predictive variables for serious events, and to define a low risk subgroup.
3. To estimate the risk of subsequent mortality due to SIDS after hospital discharge.

METHODS

STUDY DESIGN AND ETHICS APPROVAL

This study is a retrospective chart review of all patients presenting to the Emergency Department of Children's Hospital, Boston for an Apparent Life-Threatening Event between October 1995 and September 2003. This is a tertiary care pediatric hospital with an average yearly ED volume of 52,000. The institutional review board of the Children's Hospital, Boston, granted ethics approval.

CASE FINDING AND EXCLUSIONS

Cases were identified by electronically searching the assessment field of the emergency department record for the words 'apnea', 'limp', 'cyanosis', 'choke' and 'pale'. Additionally, the entire document was searched for the acronym 'ALTE' and also for 'life' within 3 words of 'event'. The search was limited to patients under 1 year of age. If a patient presented multiple times, only the first visit was entered.

Potential cases were excluded if their presenting history did not match the ALTE definition. For example, if the word 'limp' was used to refer to a musculoskeletal problem, rather than hypotonia; if a patient was assessed to have extremity cyanosis only; if the patient choked on a foreign body; or if

ALTE was mentioned in the family history and the patient presented for another reason.

DEFINITIONS AND DATA EXTRACTED

Historical

Demographic details such as age, gestational age and gender were entered into the database. Details of the event that prompted admission were coded nominally (i.e. Yes / No) for the variables color change, change in tone (limpness, stiffness), vomiting, unresponsiveness and vigorous caretaker intervention. Caretaker intervention was assessed to be vigorous if it included backblows, mouth to mouth or compressions. The duration of the ALTE was recorded if known, as was the occurrence of more than one event prior to presentation. Patients were categorized as having a significant past medical history (PMH) if they carried a specific diagnosis (e.g. gastroesophageal reflux, apnea of prematurity or tracheomalacia).

Examination

The patient was categorized as ill appearing if the Emergency Department physician described the patient using one of the following terms: 'toxic', 'ill appearing', 'lethargic', 'grey', 'weak cry', 'grunting' or 'poorly perfused'. We also recorded the presence of any pulmonary signs.

Emergency department testing

All ED testing was recorded in the database. Results were coded as either normal, abnormal clinically insignificant or abnormal clinically significant. Laboratory abnormalities were defined using a standard reference (40). Abnormal tests were categorized as 'clinically significant' if they led to a diagnosis or altered medical management. For example, although a low serum potassium concentration is abnormal, it would not be considered clinically significant if it did not alter management or lead to a diagnosis. Abnormal testing that only altered medical management by leading to subsequent normal testing (e.g. repeating the same test) was not coded as clinically significant.

ED and inpatient serious events

Serious events were defined as the occurrence of cyanosis, apnea, seizure, oxygen saturation $\leq 90\%$, limpness, unresponsiveness or death. The ED record and nursing flow chart, inpatient admit note, progress notes, nursing flow chart, and discharge summary were all reviewed to find serious events occurring during the patient's hospital visit. The time of the first event was calculated from the time the patient arrived on the inpatient unit.

Low risk group

After preliminary analysis of the first 146 cases, we defined a group at low risk for serious events. The low risk group was defined as patients who were not "ill appearing", did not have a serious event in the emergency department and were not admitted to the intensive care unit (ICU).

Diagnosis

The etiology of the ALTE was assigned using the patient's discharge diagnosis field in the medical record. If more than one etiology was listed in the discharge summary, the chart was reviewed by at least one physician researcher to determine the etiology of the event. Additionally, the discharge summary was reviewed for any other clearly documented diagnosis. For example, if the summary indicated ranitidine was prescribed and that gastroesophageal reflux was the likely cause, this would be recorded as the etiology even if it was omitted from the diagnosis field.

A list of life threatening conditions was compiled independently by the two senior authors and differences resolved by consensus of the three authors.

Subsequent Mortality from SIDS

Patients in our sample were cross-referenced with the Massachusetts Center for SIDS database. State legislation requires that all deaths in children less than two years of age be reported to the Massachusetts Medical Examiners Office. This data is then forwarded to the Center for SIDS and is compiled in a database, categorized by cause of death.

DATA EXTRACTION

Data extraction was completed by a third year medical student and a pediatric emergency medicine fellow.

Four hours of consensus building was conducted prior to beginning chart analysis, the results of which were compiled in a document of variable definitions. During data extraction, regular meetings were held to discuss problematic cases and reach a consensus on the data coding. During these meetings the senior investigator was also present and provided input. Additionally, 72 cases were co-reviewed by the senior investigator to assess reviewer consistency.

Data was entered into a Microsoft Access database.

STATISTICAL ANALYSIS

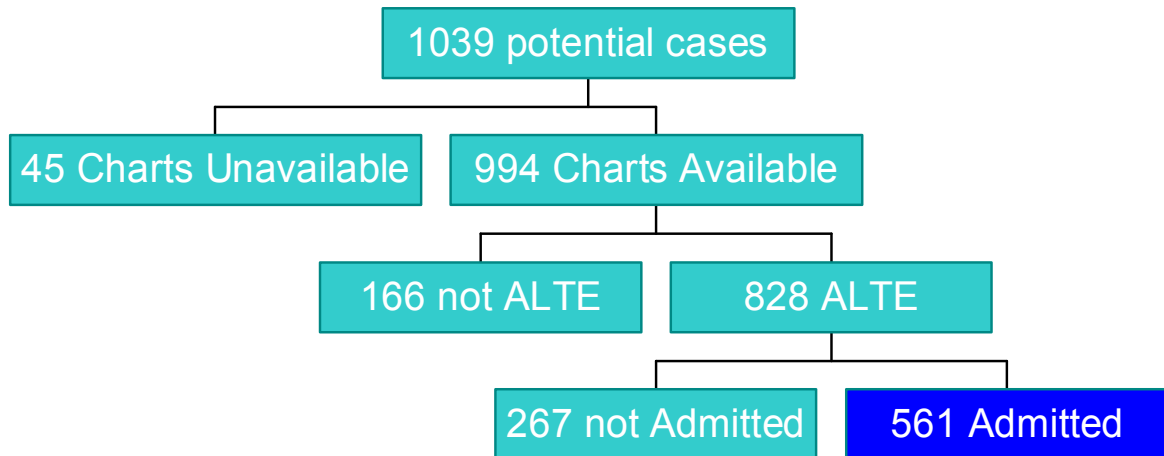
Statistical analysis was performed primarily using the Statistical Package for the Social Sciences, v11.0.1 (SPSS Inc, Chicago, IL). The Mann-Whitney U test was used for nonparametric continuous data. For nominal predictors the chi-square test for association was performed. Relative risk and 95% confidence intervals were also calculated.

The Bonferroni correction was used to adjust for the multiple comparisons used to predict serious events.

The binomial distribution was used to construct confidence intervals for proportions using Stata v7.0 (Stat Corporation, College Station, TX).

RESULTS

Figure 1: Flowchart of Patients Identified by Electronic Search



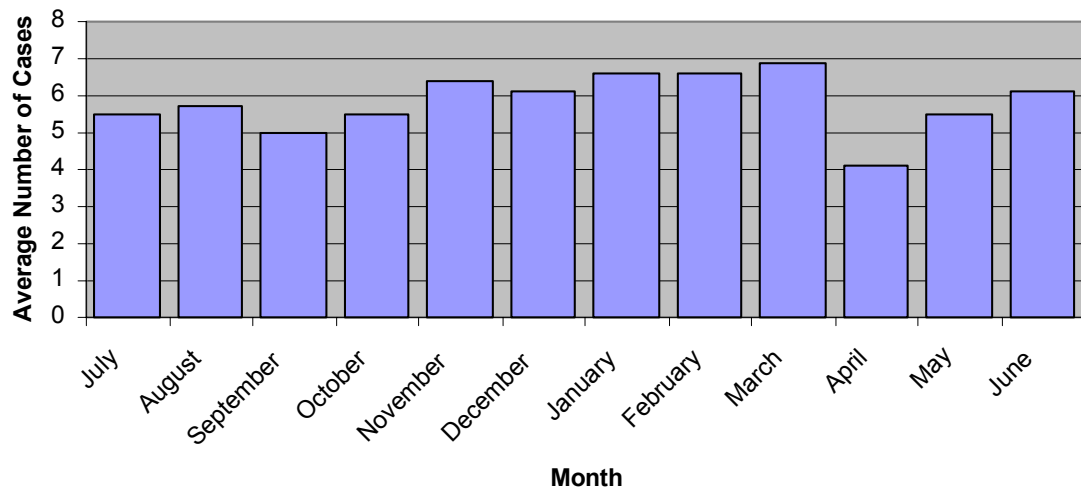
DEMOGRAPHICS

Figure 1 displays the distribution of the patients identified. 187 / 267 (70%) patients discharged from the emergency department were diagnosed with a choking episode. The 561 patients admitted for an ALTE form the study population. Basic clinical data on these patients is presented in Table 3 and the mean number of cases per month is displayed in Figure 2.

Table 3: Clinical Characteristics of Admitted Patients

Median Age (10 th and 90 th deciles)	47 days (7, 143)
Female	50%
Preterm (<37weeks)	27%

Figure 2: Mean Number of Cases per Month



SERIOUS EVENTS

Of the 561 admitted patients, 135 (24%) had serious events during their hospitalization and these events occurred after a median 7.7 hours of admission. The majority of serious events were oxygen desaturations to below 90% with some combination of apnea and cyanosis (Figure 3). Six patients had seizures during their hospitalization and two had limp and unresponsive spells. There were no deaths.

Figure 3: Characteristics of Serious Events

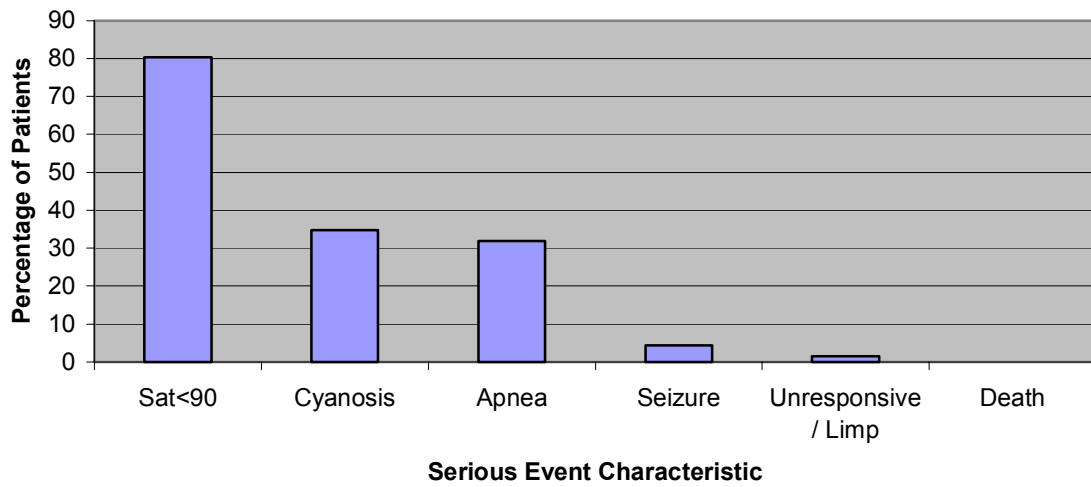


Figure 4 displays the risk of having a first serious event after the time indicated on the x-axis. Half of the patients who had a serious event did so before 7 hours of admission and only 14 patients (2.5%) had a first serious event >24 hours after admission (Table 4).

Figure 4: Risk of First Serious Event

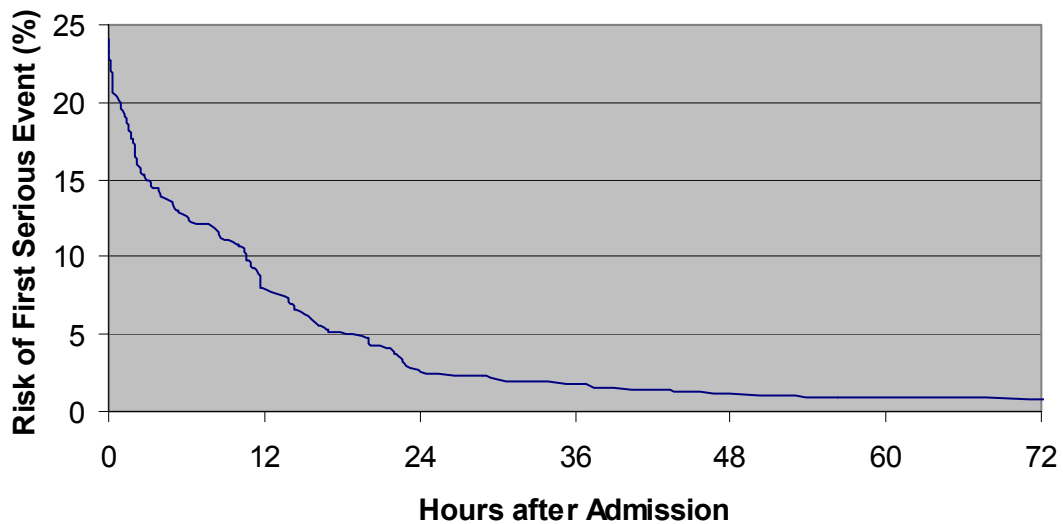


Table 4: Serious Events >24 Hours After Admission

Type of Serious Event	Details of Events / Patient	Event Time (h)	
Desaturation <90%	Predisposing PMH	▪ (2) Apnea of prematurity	12, 39
		▪ (1) Tracheoesophageal fistula and tracheomalacia	80
		▪ (1) Freeman-Sheldon Syndrome	192
	Bronchiolitis	▪ (3) With initial symptoms <24 hours	29, 31, 44
	Self-limited	▪ (2) Gastroesophageal Reflux	29, 36
		▪ (1) MCAD deficiency	25
	Other	▪ (1) Ex 29wk premature infant with PMH of ALTE. Mild desaturations at <24hours. Sleep study showed gastroesophageal reflux	52
Seizure			
	Seizure	▪ (1) Abuse with retinal hemorrhages	56
		▪ (1) Starring spells	93
		▪ (1) Multiple tonic seizures with cyanosis	43

PREDICTORS OF SERIOUS EVENTS

Comparison of the risk of serious events for those at low and high risk is shown in Table 5. The relative risk for serious events in the high risk group was 3.6 (95%CI 2.8, 4.6) and for a first serious event after 24 hours was 3.9 (95%CI 1.4, 11).

Table 5: Risk of Serious Events in the High and Low Risk Group

Group	Patients	Serious Events (%)	Events After 24 hours (%)
High Risk	91	55 (60%)	6 (6.6%)
Low Risk*	470	80 (17%)	8 (1.7%)
TOTAL	561	135 (24%)	14 (2.5%)

*Low risk criteria: Not ill appearing, no ED event and not admitted to an ICU

In addition to the ‘low risk’ criteria described above, we examined other predictors of serious events (Table 6). Results where $p < 0.05$ are shown in bold. For continuous data, younger patients ($p = 0.014$) and those with shorter events ($p = 0.099$) were less likely to have serious events, although the latter result did not achieve statistical significance.

Table 6: Univariate Predictors of Serious Events

Predictor	# patients with recorded data	Relative Risk (95%CI)	p
High Risk Group	561	3.55 (2.74, 4.60)	<0.001
Multiple Events*	561	1.84 (1.37, 2.49)	<0.001
Gestational Age <35weeks	541	1.63 (1.19, 2.25)	0.004
Significant PMH	505	1.67 (1.21,2.32)	0.015
Abnormal Tone	195	1.19 (0.579, 2.47)	0.635
Color Change	516	1.08 (0.66, 1.77)	0.770
Vigorous Caretaker Intervention	302	0.652 (0.413,1.03)	0.065
Vomiting	276	0.577 (0.352, 0.948)	0.025
Unresponsiveness	72	**	0.031

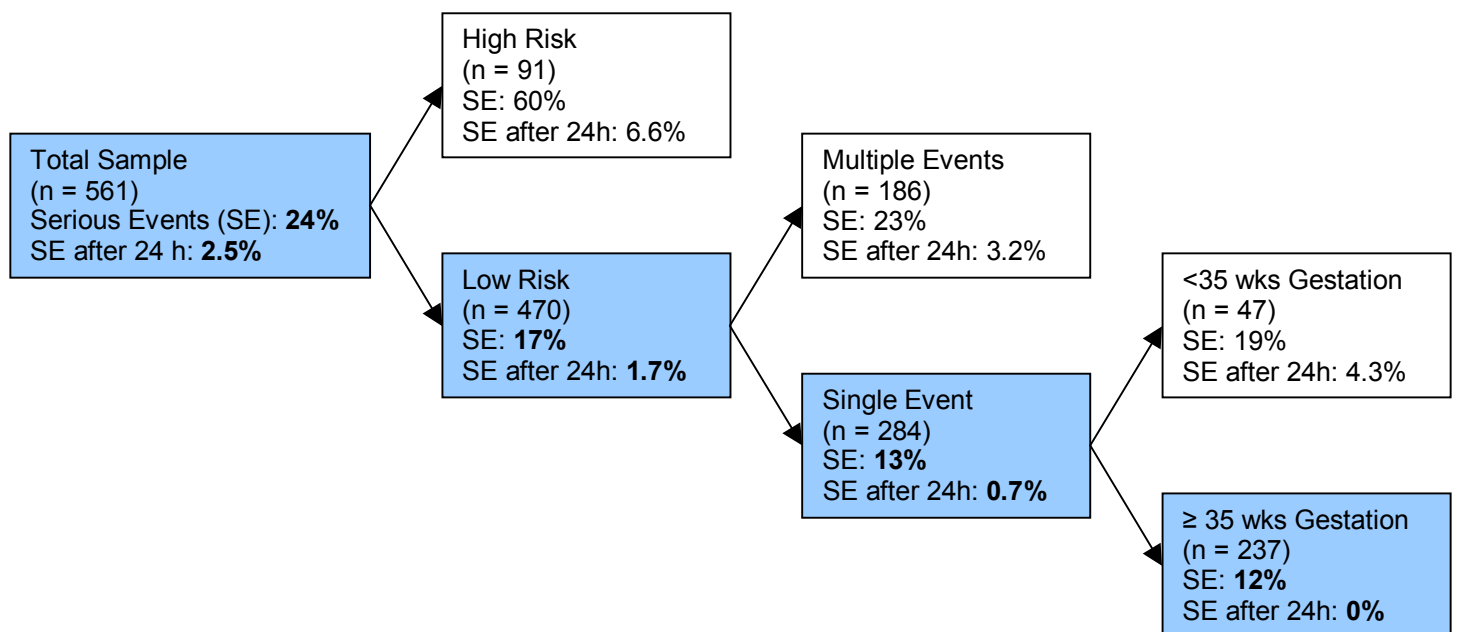
* >1 episode prior to ED visit

** no events occurred in responsive patients

When corrected for the fact that 11 comparisons were made, having multiple events, a gestation age of less than 35 weeks or being in the ‘high risk’ group retained their statistical significance as predictors of serious events.

By combining these three significant predictors we generated a risk stratification algorithm (Figure 5). None of the 237 patients (95%CI 0, 1.5%) who (a) were in the low risk group, (b) did not have multiple events at home and (c) were ≥ 35 weeks gestational age had a first serious event after 24 hours of admission.

Figure 5: Serious Event Risk Stratification Algorithm



ETIOLOGY

The discharge diagnoses of the admitted patients are presented in Table 7.

In 265 (47.3%) patients the etiology was unknown at the time of discharge.

The “other” category contains etiologies with less than 3 cases each.

Table 7: Etiological Diagnoses

Etiology	Number (%)
Gastroesophageal Reflux	157 (28%)
Bronchiolitis	45 (8.0%)
Immature Breathing Pattern	21 (3.7%)
Apnea of Prematurity	8
Periodic Breathing	8
Central Apnea	4
Immature Breathing Pattern	1
Structural Upper Airway Disease	14 (2.5%)
Laryngomalacia	3
Tracheomalacia	2
Tracheal Stenosis	2
Vocal Cord Paralysis	2
Obstructive Sleep Apnea	2
Tracheal Compression	1
Pierre-Robin Sequence	1
Upper airway Obstruction	1
Seizure	12 (2.1%)
Upper Respiratory Tract Infection	12 (2.1%)
Pertussis	8 (1.4%)
Breathholding	6 (1.1%)
Swallowing Dysfunction	5 (0.9%)
Other	28 (5.0%)
Idiopathic	265 (47%)

28 of the 561 admitted patients (5.2%) were diagnosed with a life threatening condition (Table 8).

Table 8: Life Threatening Conditions Diagnosed

Etiology	Patients
Seizure	12
Pertussis	8
Abuse	2
Bacteremia	1
Hypoglycemia	1
Intracranial Hemorrhage	1
Intussusception	1
Brain Tumor	1
MCAD Deficiency	1
Hypoparathyroidism	1

MCAD = Medium Chain Acyl-Co A Dehydrogenase

UTILITY OF EMERGENCY DEPARTMENT TESTING

518 (92%) of the patients admitted for an ALTE had at least one diagnostic test performed in the ED. 72 (14%) of these patients had at least one test that led to a diagnosis or altered management. The results for individual tests are outlined in Table 9. Results with a yield greater than 5% are shown in bold. Chest radiographs, complete blood counts, echocardiograms, electrolyte panels and blood cultures were all performed in over half of the patients admitted for an apparent life-threatening event. Of these tests, only chest radiographs had a yield above 5%. However, if this yield is stratified by the presence of any abnormal pulmonary signs (i.e. tachypnea, wheezing, rhonchi, crackles), the results displayed in Table 10 are obtained.

Table 9: Utilization and Yield of ED Diagnostic Testing

Test	Number Ordered (%)	Clinically Significant		Utility (95% CI)	Details of Abnormalities
		Abnormal	Abnormal		
Chest Radiograph	420 (75%)	23		5.5% (3.5, 8.1)	15 bronchiolitis, 4 pneumonia, 2 cardiomegaly, 1 tracheomalacia, 1 rib fracture
Complete Blood Count	407 (73%)	9		2.2% (1.0, 4.2)	4 elevated WBC count, 5 anemia
Electrocardiogram	349 (62%)	1		0.3% (0.0, 1.6)	LVI, confirmed by echocardiography as dilated cardiomyopathy
Electrolytes + Blood Urea Nitrogen /Creatinine /Glucose	316 (56%)	7		2.2% (0.01, 4.2)	3 low bicarb, 2 low glucose, 1 low bicarb / hyponatremia, 1 hyponatremia
Blood Culture	283 (50%)	1		0.4% (0.01, 2.0)	S. aureas – not contaminate
Urinalysis	192 (34%)	4		2.1% (0.6, 5.2)	4 pyuria
Urine Culture	188 (34%)	4		2.1% (0.6, 5.4)	4 urinary tract infection
Serum Calcium	162 (29%)	3		1.9% (0.4, 5.3)	1 hypocalcemia, 1 hypercalcemia, 1 hypoparathyroidism
Serum Magnesium	148 (26%)	0		0% (0.0, 2.5)	NA
Serum Phosphorus	142 (25%)	1		0.7% (0.02, 3.9)	hypoparathyroidism
Cerebrospinal Fluid Culture	131 (23%)	0		0% (0.0, 3.8)	NA
Cerebrospinal Fluid Analysis	128 (23%)	5		3.9% (1.3, 8.9)	3 traumatic, 2 pleocytosis – treated with antibiotics
Liver Function Tests	67 (12%)	4		6.0% (1.7, 15)	4 hyperbilirubinemia – treated
Neuroimaging	36 (6.4%)	2		5.6% (0.7, 19)	2 subdural hemorrhage (1 abuse)
Abdominal Radiograph	24 (4.3%)	1		4.2% (0.1, 21)	constipation
Respiratory Syncytial Virus	16 (2.9%)	5		31% (11, 59)	5 positive
Venous Blood Gas	16 (2.9%)	2		13% (1.6, 38)	2 respiratory acidosis
Arterial Blood Gas	16 (2.9%)	2		13% (1.6, 38)	1 metabolic acidosis, 1 hypoxemia
Airway Films	16 (2.9%)	4		25% (7.3, 52)	4 croup
Urine Toxicological Screen	12 (2.1%)	0		0% (0, 26)	NA
Pertussis	8 (1.4%)	3		38% (8.5, 76)	3 positive
Stool Culture	4 (0.71%)	0		0% (0, 60)	NA
Serum Toxicological Screen	3 (0.53%)	0		0% (0, 71)	NA

Table 10: Chest Radiograph Yield Stratified by Pulmonary Signs

Pulmonary Signs	Number Performed (%)	Significant Abnormal	Yield (95%CI)
Yes	34 (76%)	8	24%
No	386	15	3.9%
TOTAL	420	23	5.5%

RISK OF MORTALITY FROM SUDDEN INFANT DEATH SYNDROME

Of the 561 patients in our sample, 534 (95%) resided in Massachusetts, the capture area of the Massachusetts Center for SIDS database. One patient, with a diagnosis of spinal muscular atrophy made prior to his admission for ALTE died after hospital discharge due to complication of his disease. The estimated risk of SIDS in patients admitted for an ALTE is 0% (95% CI 0, 0.6).

DISCUSSION

Patients admitted for an ALTE are at risk of subsequent events. Our data supports prior recommendations that admission for cardiovascular monitoring and parental reassurance is appropriate. Additionally, the risk of having a serious event diminishes with the length of admission. By 24 hours the risk is sufficiently low (2.5%) that for most patients, further inpatient observation may no longer be necessary.

A minority (18%) of patients did not meet our low risk criteria and more than half of these patients had a serious event. They were 3-4 times more likely to have a serious event after 24 hours of admission. These high risk patients may need more careful or prolonged evaluations.

Additionally, infants who had more than one event prior presentation and those with a gestation age <35 weeks were at increased risk of serious events. No other historical variables reliably predicted serious events. This suggests that either these variables are of limited discriminating value, or that the association was obscured by missing data from the ED record or inaccurate reporting by a frightened observer.

As in previous studies, in our population an ALTE was the common outcome of a diverse range of causes. The proportion accounted for by each cause was in the range of values described previously. The percentage due to seizure disorders was much lower than the estimated proportion from previous research. This discrepancy may be because two studies from a

single institution (15, 16) found a higher proportion (25% and 9% respectively) than all others studies and thus skewed the estimate. The proportion in our population due to abuse (0.4%) and factious illness (0%) were also lower than previously documented. This difference may represent demographic variation, or differing physician effort in pursuing these diagnoses.

More than one in twenty patients had a life threatening condition diagnosed, confirming the need to fully evaluate infants after an ALTE.

We found a higher utility of emergency department diagnostic testing than previously described. However, the utility for most tests was still low. In fact, of the 9 diagnostic tests performed in more than 25% of our sample, only chest radiographs had a yield of >2.5%. In the appropriate subset of patients, the use of tests such as RSV antigen detection, pertussis PCR and neck and chest radiographs had a higher utility than the frequently recommended CBC, electrolytes, blood cultures and ECG (2, 17, 34).

Therefore, our findings support the idea that no battery of tests is appropriate for all patients after an ATLE. Clinical judgment should guide the appropriate utilization of diagnostic testing.

In our population, there were no subsequent deaths from SIDS. This result should allay some parental and physician concern regarding this outcome and weaken claims of a causal association.

LIMITATIONS

The usual limitations of retrospective chart reviews apply to our study. Our case identification may have been incomplete, especially for cases in which the etiology was determined in the ED. Some data was unavailable in a large number of patients, particularly for variables describing the event that prompted presentation. Also, our assessment of testing utility was limited to alterations in management that were documented in the chart.

The study was conducted in a single, tertiary care institution and the results require validation at other centers.

Our determination of etiology is potentially biased. Using the discharge summary from the initial admission limits the time available for etiology to be determined. As outlined by Nunes and colleagues (41), some of the ALTEs caused by a seizure disorder may be mistakenly ascribed to another etiology because the correct diagnosis cannot be established prior to discharge. This may also be true of other etiologies.

The proportion due to gastroesophageal reflux may be falsely elevated and merely represent the co-morbidity of a common disease in infants. Some authors have questioned the causal role of reflux in apnea (6, 42), or demonstrated that apnea may cause reflux (43).

Some of the patients in our sample were admitted for less than 24 hours. Thus our determination of the risk of events after this time may be spuriously depressed.

Our capture of deaths from SIDS may have been incomplete, as we could not account for patients who moved away from the Centre for SIDS capture area. Also, a small number of the patients enrolled in the later stages of the study may still be at risk of SIDS at the time of publication.

FUTURE DIRECTIONS

A prospective study with a standard data collection form and a standard evaluation might be able to more clearly define the etiology of these events and validate our proposed risk criteria. The use of multivariate techniques could better delineate the independent contribution of each of our proposed risk factors. Telephone follow-up would also better determine morbidity and mortality after discharge.

CONCLUSIONS

After admission for an apparent life-threatening event, almost one in four infants will have a serious event during hospitalization, but these events occur early in the admission. Since 97.5% of serious events occurred within 24 hours of admission, an admission of 24 hours may be adequate to safely evaluate most infants.

More than one in twenty patients had a life threatening condition diagnosed. This confirms the need to fully evaluate infants after an ALTE, although approximately half of all cases remain idiopathic.

The yield of emergency department testing was low, especially for those tests routinely performed.

The risk of subsequent mortality from SIDS is very low.

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